nucleotides, at least 30 nucleotides, at least 50 nucleotides, at least 100 nucleotides, at least 250 nucleotides, and at least 500 nucleotides in length (as appropriate for the length of the sequence of SEQ ID NOS:55, 62, 66, and 68, or variants thereof).

In particularly preferred embodiments, the polynucleotide hybridizes specifically to telomerase sequences, wherein the telomerase sequences are selected from the group consisting of human, *Euplotes aediculatus*, *Oxytricha, Schizosaccharomyces*, and *Saccharomyces* telomerase sequences. In other preferred embodiments, the present invention provides polynucleotide sequences comprising the complement of nucleic acid sequences selected from the group consisting of SEQ ID NOS:55, 62, 66, and 68, or variants thereof. In yet other preferred embodiments, the present invention provides polynucleic acid sequences that hybridize under stringent conditions to at least one nucleic acid sequence selected from the group consisting of SEQ ID NO:55, 62, 66, and 68. In a further embodiment, the polynucleotide sequence comprises a purified, synthetic nucleotide sequence having a length of about ten to thirty nucleotides.

In alternative preferred embodiments, the present invention provides polynucleotide sequences corresponding to the human telomerase, including SEQ ID NOS:173 and 224, and their complementary sequences. The invention further contemplates fragments of these polynucleotide sequence (*i.e.*, SEQ ID NOS: 173 and 224) that are at least 5 nucleotides, at least 20 nucleotides, at least 100 nucleotides, at least 250 nucleotides, and at least 500 nucleotides in length. The invention further contemplates fragments of the complements of these polynucleotide sequences (*i.e.*, SEQ ID NOS: 173 and 224) that are at least 5 nucleotides, at least 20 nucleotides, at least 100 nucleotides, at least 250 nucleotides, and at least 500 nucleotides in length. In addition, the invention features polynucleotide sequences that hybridize under stringent conditions to SEQ ID NOS: 173 and 224, and/or fragments, and/or the complementary sequences thereof. The present invention further contemplates a polynucleotide sequence comprising the complement of the nucleic acids of SEQ ID NOS: 173 and 224, or variants thereof. In a further embodiment, the polynucleotide sequence comprises a purified, synthetic nucleotide sequence corresponding to a fragment of SEQ ID NOS: 173 and 224, having a length of about ten to thirty nucleotides. The present invention further provides plasmid pGRN121 (ATCC accession ##20916), and the lambda clone 25-1.1 (ATCC accession # 209024 A).

The present invention further provides substantially purified polypeptides comprising the amino acid sequence comprising SEQ ID NOS:174-223 and 225. In another embodiment, the present invention also provides purified, isolated polynucleotide sequences

Figure 52 provides a refined restriction and function map of plasmid pGRN121.

Figure 53 provides the nucleic acid (SEQ ID NO:224) and deduced ORF sequence (SEQ ID NO:225) of human telomerase.

Figure 54 provides a restriction map of lambda clone 25-1.1 (ATCC accession #209024).

DEFINITIONS

To facilitate understanding the invention, a number of terms are defined below.

As used herein, the term "ciliate" refers to any of the protozoans belonging to the phylum Ciliaphora.

As used herein, the term "eukaryote" refers to organisms distinguishable from "prokaryotes." It is intended that the term encompass all organisms with cells that exhibit the usual characteristics of eukaryotes such as the presence of a true nucleus bounded by a nuclear membrane, within which lie the chromosomes, the presence of membrane-bound organelles, and other characteristics commonly observed in eukaryotic organisms. Thus, the term includes, but is not limited to such organisms as fungi, protozoa, and animals (*e.g.*, humans).

As used herein, the term "polyploid" refers to cells or organisms which contain more than two sets of chromosomes.

As used herein, the term "macronucleus" refers to the larger of the two types of nuclei observed in the ciliates. This structure is also sometimes referred to as the "vegetative" nucleus. Macronuclei contain many copies of each gene and are transcriptionally active.

As used herein, the term "micronucleus" refers to the smaller of the two types of nuclei observed in the ciliates. This structure is sometimes referred to as the "reproductive" nucleus, as it participates in meiosis and autogamy. Micronuclei are diploid and are transcriptionally inactive.

As used herein, the term "ribonucleoprotein" refers to a complex macromolecule containing both RNA and protein.

As used herein, the term "telomerase polypeptide," refers to a polypeptide which is at least a portion of the *Euplotes* telomerase structure. The term encompasses the 123 kDa and 43 kDa polypeptide or protein subunits of the *Euplotes* telomerase. It is also intended that the term encompass variants of these protein subunits. It is further intended to encompass the polypeptides encoded by SEQ ID NOS: 1 and 3. As molecular weight measurements may

To obtain a full-length clone, probing of a cDNA library and 5 '-RACE were used to obtain clones encoding portions of the previously uncloned regions. In these experiments, RACE (Rapid Amplification of cDNA Ends; *See e.g., M.A.* Frohman, "RACE: Rapid Amplification of cDNA Ends," *in* Innis *et al.* (eds), *PCR Protocols: A Guide to Methods and Applications* [1990], pp. 28-38; and Frohman *et al.*, Proc. Natl. Acad. Sci., 85:8998-9002 [1988]) was used to generate material for sequence analysis. Four such clones were generated and used to provide additional 5' sequence information (pFWRP5, 6, 19, and 20).

In addition, human cDNA libraries (inserted into lambda) were probed with the EcoRI-NotI fragment of the clone (#AA281296). One lambda clone, designated "lambda 25-1.1," (ATCC accession #209024) was identified as containing complementary sequences. Figure 54 shows a restriction map of this lambda clone. The human cDNA insert from this clone was subcloned as an *Eco*RI restriction fragment into the *Eco*RI site of commercially available phagemid pBluescriptIISK+ (Stratagene), to create the plasmid "pGRN121," which was deposited with the ATCC (ATCC accession #209016). Preliminary results indicated that plasmid pGRN121 contains the entire open reading frame (ORF) sequence encoding the human telomerase protein.

The cDNA insert of plasmid pGRN121 was sequenced using techniques known in the art. Figure 49 provides a restriction site and function map of plasmid pGRN121 identified based on this preliminary work. The results of this preliminary sequence analysis are shown in Figure 50. From this analysis, and as shown in Figure 49, a putative start site for the coding region was identified at approximately 50 nucleotides from the *Eco*RI site (located at position 707), and the location of the telomerase-specific motifs, "FFYVTE" (SEQ ID NO:112), "PKP," "AYD," "QG", and "DD," were identified, in addition to a putative stop site at nucleotide #3571 (*See,* Figure 51). Figure 51 shows the DNA and corresponding amino acid sequences for the open reading frames in the sequence ("a" [SEQ ID NOS:174-201], "b" [SEQ ID NOS:202-214], and "c" [SEQ ID NOS:215-223]). However, due to the preliminary nature of the early sequencing work, the reading frames for the various motifs were found not to be in alignment.

Additional analysis conducted on the pGRN121 indicated that the plasmid contained significant portions from the 5'-end of the coding sequence not present on the Genbank accession #AA281296 clone. Furthermore, pGRN121 was found to contain a variant coding sequence that includes an insert of approximately 182 nucleotides. This insert was found to be absent from the Genbank accession #AA281296 clone. As with the *E. aediculatus*